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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/617,099	07/14/2000	Susumu Seino	P19771	5279

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Greenblum & Bernstein P L C
1941 Roland Clarke Place
Reston, VA 20191

EXAMINER
MITRA, RITA

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/617,099	SEINO ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 July 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1653.

Applicants' request in paper NO: 10 filed on January 8, 2002 for remailing of office action dated December 18, 2001 is acknowledged. The Preliminary Amendment filed concurrent with the application has been considered and entered in paper NO: 2 and1/2. Therefore, the office action dated December 18, 2001 is vacated and following new office action is prepared. The three-month shortened statutory period for responding to the December 18, 2001 office action will restart from the date of mailing of this new office action.

Election/Restriction

Applicants' election with traverse of Group II (claims 3-12) in paper #8 (filed on November 1, 2001) is acknowledged. The traversal is on the ground that Group I (protein), Group II (DNA) and Group IV (Diagnostic agent) are similar in their concepts, thus, a search for the DNA of Groups II and IV should cover areas relevant to the protein of Group I. In addition Applicants urge that a search for the antibodies of Groups III and V should cover areas relevant to the protein of Group I, therefore the searches for the groups should significantly overlap and the search burden would not be serious. The traversal has been fully considered and not found persuasive because Groups I, II, IV and Groups I, III, V are directed to different subject matter as shown by different classification across the groups. Additionally, the issue of the subject matter of each Group is different. Therefore, examination of all groups would present a search burden, because the searches of both the patent and non-patent technical literature are not co-extensive. For example, a search for the DNA does not result in a search of all literature for the protein nor the antibody (ies). In addition, a protein and a DNA cannot be substituted one for the other as

each has different physical, chemical, and biological properties and functions. As to the commentary regarding filing fees, filing fees are not a criteria for non-restriction. Furthermore, applicants indicate that it was not stated in the office action that a definition of what is "materially different." Applicants' attention is drawn to the page 3 of the office action dated October 1, 2001 where a definition of "materially different process" has been indicated clearly.

The restriction requirement is still deemed proper and is therefore made **FINAL.**

Claims 1, 2 and 13-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention. Therefore, claims 3-12 are currently pending and are under examination.

Priority

Applicant's claim for foreign priority under 35 U.S.C. 119 (a-d) is acknowledged. This application claims a priority of a Japanese Application No. 11-288372, filed on October 8, 1999. Although, the instant application has provided a copy of this application, it fails to provide a certified copy of English translation in support of the priority date claimed. Therefore, the priority date granted is July 4, 2000, which is a filing date of this application.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3, 5-7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims recite a "gene" and "DNA" which reads on the natural, non-patentable, state of the DNA as for example in a mouse (claim 3+). The rejection would be overcome by the insertion of language indicating that the gene and DNA was isolated and/or purified, thus being removed from the natural environment.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Insofar as claim 3 amended depends from claim 1, claim 3has been read in independent format incorporating all the limitations of claim 1.

Claims 3-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a full length DNA set forth in SEQ ID NO: 2 encoding the protein of SEQ ID NO: 1; does not reasonably provide enablement for all mutants or fragments generated from any position located on the sequence of SEQ ID NO: 1 or SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 3-12 encompass a gene that encodes a protein having the amino acid sequence set forth in SEQ ID NO: 1 (claim 3), a DNA having a nucleotide sequence set forth in SEQ ID NO: 2(claims 4 and 6), a DNA having a nucleotide sequence with one or more nucleotides deleted, substituted, inserted or added relative to the nucleotide sequence set forth in SEQ ID NO: 2 (claims 5, 7), a fragment of nucleotide sequence set forth in SEQ ID NO: 2 (claim 8), a probe comprising a DNA which hybridizes with the DNA of SEQ ID NO: 2 (claim 9), a primer DNA fragment consisting of a partial sequence of the sequence of the sequence of SEQ ID NO: 2 (claim 10,), a recombinant vector having the DNA of SEQ ID NO: 2 (claim 11), a vector having the mutant generated from SEQ ID NO: 2 (claim 12). The specification, however, only discloses cursory conclusions (see page 4-5), without data to support the findings, which state that a mouse gene that encodes the protein of SEQ ID NO: 1. and a mutant thereof, which has a property of interacting with a GDP/GTP exchange factor II. The specification. There are no indicia that the

present application enables the full scope in view of the gene encoding the protein of SEQ ID NO: 1 and a mutant thereof as discussed in the following stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is encompassed.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: 1) the nature of the invention; 2) the breadth of the claims; 3) the predictability or unpredictability of the art; 4) the amount of direction or guidance presented; 5) the presence or absence of working examples; 6) the quantity of experimentation necessary; 7) the state of the prior art; and, 8) the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

1) the nature of the invention:

The nature of the invention is defined by the claims, which include a mouse gene encoding a protein set forth in SEQ ID NO: 1 and a mutant thereof. However the specification does not provide the information on the structure and function of the claimed mutants.

2) the breadth of the claims:

The breadth of the claims is broad and encompasses an unspecified amount of variants regarding the gene's protein products of SEQ ID NO: 1 as biological active fragments, which are not specifically described or demonstrated in the specification.

Claim 3 is drawn to a mouse gene that encodes the protein of SEQ ID NO: 1. Specification on pages 4-5 gives a description about a mouse gene that encodes a protein having an amino acid sequence set forth in SEQ ID NO: 1 and a mutant thereof, which has a property of interacting with a GDP/GTP exchange factor II. The specification does not provide a sequence of a gene, where gene means genomic DNA encoding a protein. It is art recognized that a gene includes promoters and other regulatory elements as well as exons and introns. There are no

indicated regulatory sequence(s) necessary for the expression of this gene nor there is any sequence of untranslated region that are described. SEQ ID NO: 2 is a cDNA sequence hence it contains only exons. There is no disclosure of the introns nor what the intron sequences are nor what the regulatory elements are and one skilled in the art would not have known the nucleic acid sequence. For these reasons, it requires undue experimentation to make the claimed invention, especially where in claim 5, any one or more nucleotides, singly or in any combination of insertion, deletion and substitution would have been included by the claim and for which the specification does not describe with particularity as to retention of function.

Claim 5, and the dependent claims 7 and 12 thereto, which are directed to a DNA having a nucleotide sequence with one or more nucleotides deleted, substituted, inserted or added relative to the nucleic acid sequence set forth in SEQ ID NO: 2 and a recombinant vector having the said modified DNA sequence. Specification while defining "one or more" indicates at page 5 that several (e.g. 3 or 4) to 10 nucleotides relative to SEQ ID NO: 2 would be modified, and at page 7 specification provides a general description on how a variety of mutants can be generated. However, the specification fails to provide any specific description of the structure and function of the mutants generated. While the specification in Example (page 14, lines 15-22, Fig. 4), and at page 9, lines 4-16 describes and demonstrates that the full length DNA set forth in SEQ ID NO: 2 encoding the protein of SEQ ID NO: 1 has a property to interact with cAMP-GEFII, there is no disclosure about the biological activities of the claimed mutants. For the reasons set forth above, undue experimentation is necessary to make and use the claimed mutants encoding a protein that retains the property of interacting with cAMP-GEFII.

Claim 8 is directed to a fragment of a DNA sequence set forth in SEQ ID NO: 2. The specification fails to provide any description of the structure and function of the fragment claimed. While the specification at page 5 defines the fragment as a DNA fragment consisting of a part of any one of the DNAs set forth in full length sequence set forth in SEQ ID NO: 2or in the mutant sequence thereof, however, there is no disclosure about the biological activities of the claimed fragments. Without any guidance or suggestions a skilled artisan would not be able to predict the structure of a fragment that would demonstrate the same activity as the activity of the

full length DNA sequence of SEQ ID NO: 2. Thus, for the reasons set forth above, undue experimentation is required to make and use the claimed fragments.

Claim 9 is directed to a probe comprising a DNA sequence that hybridizes to the DNA sequence set forth in SEQ ID NO; 2. Applicants have not sufficiently defined the specific conditions of stringency under which the hybridization is to take place. While describing Northern Blot and *In situ* hybridization at page 5 the specification indicates the sequence of the probe in lines 1-4 and 9-14, however, specification fails to provide the hybridization conditions. Therefore it requires undue experimentation to practice the invention.

Claim 10 is directed to a primer consisting of a partial sequence of the DNA sequence set forth in SEQ ID NO; 2. Specification fails to provide the specific sequence of the primer that would anneal to the DNA template of a sequence set forth in SEQ ID NO: 2. Therefore it requires undue experimentation to design and develop a suitable primer for practicing the invention given the current claim.

3) the predictability or unpredictability of the art;

The invention is highly unpredictable for the reasons set forth for factors 1 and 2 above.

As to factors 4 through 6, ((4)the amount of direction or guidance presented; 5) the presence or absence of working examples; and, 6) the quantity of experimentation necessary)) the claims are directed to a mouse gene that encodes the protein of SEQ ID NO: 1 and a mutant thereof; and a DNA sequence set forth in SEQ ID NO: 2 corresponds to protein of SEQ ID NO: 1 and fragments thereof. However, the specification provides only a generic description of how a variety of mutants can be generated (page 7), no specific guidance is provided on the generation of the mutants or fragments that demonstrate the biological activity of the full length protein or DNA sequences. There are no working examples of these variants in the specification. While the specification in Example (page 14, lines 15-22, Fig. 4), and at page 9, lines 4-16 describes and demonstrates that the full length DNA set forth in SEQ ID NO: 2 encoding the protein of SEQ ID NO: 1 is asserted to interact with cAMP-GEFII, there is no

disclosure about the biological activities of the claimed mutants. Since the specification fails to provide sufficient guidance on the structure and function of the various mutants and fragments, it is necessary to have additional guidance on the identities of mutants/fragments to carry out further experimentation to assess their property of interacting with cAMP-GEFII.

4) the state of the prior art; and,

5) the relative skill of those skilled in the art:

The prior art has shown a cDNA with 5640 bp from a rat brain library, which encodes a large protein RIM2 with 1555 amino acid residues, RIM2 cDNA has 75.8% sequence identity to SEQ ID NO: 2 (see section below of 102/103 (a) rejection), however, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the structure and function for various protein/ DNA products to be considered enabling for variants.

In consideration of each of factors 1 – 8, it is apparent that there is undue experimentation because in summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants, the guidance/the teaching in the specification is limited, and the outcome is unpredictable for the various modified forms, it is necessary to have additional guidance and to carry out further experimentation to assess the property of the variants. Therefore, due to large quantity of experimentation necessary to determine an activity or property of the disclosed gene and the modified forms thereof, such that it can be determined how to use the claimed gene, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the specification fails to teach the skilled artisan how to make and use the claimed invention.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

"The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

Claims 3-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-12 appear to broaden the scope of claim 3 by inclusion of terminology such as "corresponding to" (claim 4), and "one or more nucleotides deleted, substituted, inserted or added relative to the nucleotide sequence...". The function of a dependent claim is to limit, i.e., more narrowly define the invention. The current claims do not do this and are therefore indefinite by increasing the bounds of the claim(s).

Claims 3-5 and claims dependent thereto are rejected as being dependent upon non-elected claims. In addition it is suggested that claim 3 incorporate "SEQ ID NO: 1" into the claim. Claim 4 is indefinite with regard to "cDNA corresponding to the proteins..." because it is not apparent how a cDNA (a polynucleotide) corresponds to a protein. There is no correspondance per se but the cDNA can "encode" the protein (see language of claim 5).

Claims 4 and 5 are indefinite because of the term "under." The term "under" renders the claim indefinite. It is not clear whether or not the nucleotide sequence is encompassed by SEQ ID NO: 2. A replacement of term "under" with "of" would overcome this rejection. Claims 6, 7, 11 and 12 are included in the rejection because they are dependent upon a rejected claim and do not correct the deficiency of the claim from which they depend.

Claims 5 is indefinite because of the phrase "one or more." The phrase "one or more" renders the claim indefinite. It is not clear how many nucleotides are deleted, substituted, inserted, or added relative to the nucleotide sequence set forth in SEQ ID NO: 2, which has 4980 nucleotides. Furthermore, the position of these nucleotides in relation to the sequence of SEQ ID NO: 2 is also not clear. Claim 7 is included in the rejection because they are dependent upon a rejected claim and do not correct the deficiency of the claim from which they depend.

Claims 6 and 7 lack antecedent basis for "the coding region" in claim 4 nor is it apparent in claims 6 and 7 how they further limit claims 4 and 5 since each appears to have the same sequence and length.

Claim 8 is indefinite as to what part is the part that claim 8 refers to that is from claim 4.

Claim 10 is indefinite because of the term "partial sequence." The term "partial sequence" renders the claim indefinite. It is not clear how many nucleotides are there in this partial sequence that the primer consist of. Also what is the position of the primer sequence relative to the sequence of claims 4-7?

Claim Rejections – 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Insofar as claim 3 amended depends from claim 1, claim 3 has been read in independent format incorporating all the limitations of claim 1.

Claims 4-12 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Wang et al. (J. of Biol. Chem. vol. 275 (26), pp 20033-20044, June 30, 2000). Wang et al. teach a cDNA with 5640 bp from a rat brain library, which encodes a large protein RIM2 with 1555 amino acid residues (see page 20035, col. 2, under "Identification and Molecular Cloning of RIM2," and Fig. 1, page 20036). RIM2 cDNA has 75.8% sequence identity to SEQ ID NO: 2 (see sequence alignment result, GenEmbl database, Accession NO: AF199322, July 4, 2000). This reads on claims 4, 5 and 7, which has any number of insertions, deletions and/or substitutions both singly and/or in any combination. See the sequence alignment attached to the Wang et al. reference. Claim 4 is also rejected because absent factual evidence to the contrary, the reference discloses a DNA that corresponds to DNA encoding the protein. Since claim 6 only requires a claim 4 DNA corresponding to a protein of claim 1 (i.e. does not require 100% amino acid sequence identity) thus, absent factual data to the contrary it would have been obvious that the reference disclosed DNA encoding a protein corresponding to the protein of claim 1. As to claim 8, the Wang et al. reference discloses fragments that are/would have been those fragments that consist of part of the DNA of claim 4. The issue of the claim 9 probe is disclosed at page 20035, right column, under 'RNA Blotting Experiments' of the reference. As to primers, the claim 10 primer is to hybridize to the DNA of claim 4, which any DNA corresponding to the protein of claim 1. The Wang et al. reference discloses such DNA encoding a protein corresponding to the protein of claim 1, thus it is anticipated if not obvious that the strand complementary to the coding strand would have been a primer. The claims 11 and 12 vectors are set forth at page 20034 right column.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rita Mitra, Ph.D.
March 24, 2002

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600